REMARKS

This is responsive to an Office Action mailed on October 9, 2007. The Office Action finally rejected claims 1-35. Applicants have amended claim 31, canceled claim 22, and added new claim 36. The application currently includes claims 1-36.

Support for new claim 36 is found at least at page 24, line 25 – page 26, line 15. Support for the amended claim language in claim 31 is found at least at page 2, lines 19-24 and page 18, line 6 – page 24, line 23.

The Office Action rejected claims 1-35 under 35 U.S.C. §103(a) as being unpatentable over Carlyle et al. International Publication No. WO 99/37337 (the Carlyle application) in view of U.S. Patent No. 6,124,131 (the Semenza patent) or Tsuzuki et al. (the Cancer Research Article). The Office Action alleges that the Carlyle application teaches a medical device onto which VEGF has been attached to promote population of the device with viable cells and other positive results. The Office Action further alleges that the Carlyle application teaches all the claimed devices in detail through the reference and also details means for attaching the peptide to the device in all of the methods Applicants claim. The Office Action further alleges that the Carlyle application teaches all of the claimed limitations except that the reference uses VEGF and does not teach using a VEGF stimulation compound. The Office Action then alleges that at the time that the invention was made, it would have been obvious to one of ordinary skill in the art to substitute a known VEGF stimulation compound for the VEGF used by the Carlyle application because such a compound would cause the production of a desired compound VEGF.

The Office Action states that the Carlyle application does not teach using HIF-1α as the stimulator/agonist of VEGF. However, the Office Action alleges that it would have been obvious at the time the invention was made to use HIF-1α in lieu of VEGF in the process disclosed in the Carlyle application or device disclosed in the Carlyle application because the Semenza patent and Cancer Research Article teach that HIF-1α is a known stimulator of VEGF.

The Office Action concludes that there was a reasonable expectation that substituting HIF-1α for the VEGF in the invention of Carlyle would produce like results. The Office Action also states that the references clearly indicate that the various proportions and amounts of the

ingredients used in the claimed device are result effective variables, and as such, they would be routinely optimized by one of ordinary skill in the art practicing the invention disclosed by those references. The Office Action also states that general differences in concentration or other similar experimental variables will not support the patentability of the subject matter encompassed by the prior art unless there is evidence indicating such differences are critical.

Applicants respectfully disagree that utilizing HIF-1α as a stimulator agonist or attaching VEGF produce the same results. Contrary to the allegations contained in the Office Action, the Application is replete with references disclosing the advantages of utilizing HIF-1α to produce VEGF instead of coating a medical device with VEGF which are listed below.

For instance, the reasons or advantages include, but are not limited to:

> The HIF and/or other stimulation compounds direct natural processes that encourage cellular activity and vascularization near the medical device without the effort associated with in vitro manipulation of cells.

Page 5, lines 19-21.

> Incorporation of a stimulation molecule capable of stimulating VEGF production near the surface of a medical device, such as a heart valve prosthesis, or a portion thereof, could reduce the risk of thrombosis and the long-term need for anticoagulation therapy.

Page 6, lines 2-5.

> The stimulation compound generally is releasably associated with the biocompatible material such that the stimulation compound is gradually released into the fluids and/or tissue surrounding the medical device.

Page 18, lines 8-10.

> While the stimulation compound stimulates the generation of VEGF in the vicinity of the biocompatible material, it may be desirable to also have VEGF associated with the biocompatible material. ... Thus, the combined use of an associated stimulation compound and associated VEGF can have a synergistic effect with

respect to promoting the colonization of the biocompatible material.

Page 25, lines 5-7, 13-15.

> In other embodiments, a portion of biocompatible material with associated stimulation compounds is placed in a cell culture system as a time release agent to gradually release stimulation compound into the cell culture. Stimulation compound could be desirable in the cell culture system to provide a constant regeneration of VEGF through cellular activity.

Page 28, line 30 – page 29, line 2.

Therefore, associating a stimulation compound with a medical device to produce VEGF clearly does not produce the same results as coating a medical device with VEGF as alleged in the Office Action. Therefore, the allegations that the same results would likely be reproduced by utilizing HIF-1α is to stimulate VEGF instead of coating with VEGF have been addressed and refuted.

Further, utilizing a stimulation compound to produce VEGF on a prosthesis is not the same and does not produce the same results as merely coating a prosthesis with VEGF for the reasons stated above, including but not limited to, providing a constant regeneration of VEGF through cellular activity and an associated stimulation compound and associated VEGF can have a synergistic effect with respect to promoting the colonization of the biocompatible material. A constant regeneration of VEGF and a synergistic effect in promoting colonization of the biocompatible material is different than a coating VEGF on a prosthesis as disclosed in the Carlyle application. Therefore, utilizing a stimulation compound to produce VEGF is not a matter of routine optimization or a difference in concentration as alleged in the Office Action.

In contrast to utilizing HIF-1α as a stimulation compound on a prosthesis as claimed, the Semenza patent and the Cancer Research Article disclose the discovery that HIF-1α promotes VEGF production. There is no disclosure in either the Semenza patent or the Cancer Research Article of utilizing the discovery that HIF-1α promotes VEGF production with an implantable prosthesis. Therefore, the combination of the Carlyle application with either the Semenza patent and the Cancer Research Article does not make claim 1 obvious.

For the foregoing reasons, claim 1 is in allowable form. Reconsideration and allowance of claim 1 are respectfully requested.

Claims 2-30 depend from independent claim 1 and were rejected for the reasons stated with respect to claim 1. While Applicants do not acquiesce to the rejection, the rejection has been overcome for the reasons stated with respect to the allowability of claim 1. Reconsideration and allowance of claims 2-30 are respectfully requested.

The Office Action also rejected independent claim 31 as being obvious for the reasons stated with respect to claim 1. For the reasons stated with respect to claim 1, claim 31 is not obvious and also is in allowable form.

Further, claim 31, as amended, claims that the stimulation compound is released from the medical device over time to stimulate the production of growth factor such that the colonization of the medical device with endothelial cells is promoted for a greater amount of time as compared to associating the growth factors with the medical device without the stimulation compound.

There is no disclosure in the Carlyle application of associating a stimulation compound to a medical device. Further there is no disclosure of releasing the stimulation compound over time to promote the colonization of the medical device with endothelial cells. The Cancer Research article and the Semenza patent disclose the discovery that HIF-1α promotes VEGF. Neither reference discloses utilizing HIF-1α on a medical device. Therefore, the cited references do not make claim 31 obvious. Reconsideration and allowance of claim 31 are respectfully requested.

Claims 32-35 depend from independent claim 31 and were rejected for the reasons stated with respect to claim 31. While Applicants do not acquiesce to the rejection, the rejection has been overcome for the reasons stated with respect to the allowability of claim 31. Reconsideration and allowance of claims 32-35 are respectfully requested.

Applicant has added new claim 36 to the application which is allowable over the cited prior art for the reasons stated with respect to claim 1. Further, associating both the growth factor and the stimulation compound to the medical device produces synergistic effects regarding the promotion of colonization of the medical device with viable cells. See page 24, line 25 – page 26, line 15. Therefore, claim 36 is allowable over the cited prior art.

The Director is authorized to charge any fee deficiency required by this paper or credit any overpayment to Deposit Account No. 23-1123.

Respectfully submitted,

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